NDA 18-354/S-03 8

The R.W. Johnson Pharmaceutical research Institute
Attention: Donna Panasewicz
Director, Regulatory Affairs
920 Route 202 South
P. 0. Box 300
Raritan, NJ 08869-0602

Dear Ms. Panasewicz:

Please refer to your supplemental new drug application dated March 22, 1999, received March 23, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ORTHO-NOVUM® 10/11 21 & 28 (norethindrone/ethinyl estradiol) Tablets.

We note that this supplement was submitted as a 'Special Supplement - Changes Being Effected' under 21 CFR 314.70(c).

This supplemental new drug application provides for the following text modification to the *liver tumors* section in the Brief Summary, **Patient Package Insert, for the** 28 day DIALPAK:

From:

2. "Liver tumors, which may rupture and cause severe bleeding. A possible but not definite association has been found with the pill and liver cancer. However, liver cancers are extremely rare. The chance of developing liver cancer from using the pill is thus even rarer."

To:

2. "In rare cases, oral contraceptives can cause benign but dangerous liver tumors. These benign liver tumors can rupture and cause fatal internal bleeding. In addition, some studies report an increased risk of developing liver cancer. However, liver cancers are rare."

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted final printed labeling (patient package insert submitted March 22, 1999. Accordingly, the supplemental application is approved effective on the date of this letter.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MED WATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Jennifer Mercier, Regulatory Project Manager, at (301) 827-4260. Sincerely,

Susan Allen, M.D., M.P.H.
Acting Director
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research